IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICANT

: Young et al.

INVENTION:

: CYTOTOXICITY MEDIATION OF CELLS

EVIDENCING SURFACE EXPRESSION OF CD44

SERIAL NUMBER

•

FILING DATE

: (Filed Herewith)

EXAMINER:

:

GROUP ART UNIT

•

ATTORNEY DOCKET NO.

: 2056.025

INFORMATION DISCLOSURE STATEMENT

Mail Stop Patent Applications Commissioner for Patents 2011 S. Clark Place Crystal Plaza 2, Lobby RM 1 B03 Arlington, VA 22202

Sir:

Pursuant to the Duty to Disclose under 37 C.F.R. §1.56, the references cited on the accompanying form PTO-1449 are hereby brought to the attention of the Examiner for independent evaluation. A copy of each reference is enclosed. The references were cited in the specification and their relevancy is set forth therein.

Applicants submit that the present invention is patentable over these references.

Date: 8/22/2003

Respectfully Submitted,

Ferris H. Lander

Reg. No. 43,377

McHale & Slavin, P.A.

2855 PGA Boulevard

Palm Beach Gardens, FL 33410

Telephone: (561) 625-6575

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

		itute for form 1449/PT		no porsono are reganda te		ntion unless it contains a valid OMB control number mplete if Known
					Application Number	
	INI	CODMATIC	M DISC	OSLIDE	Filing Date	Herewith
			_		First Named Inventor	David S. F. Young
	ST				Art Unit	
		(Use as many	PRMATION DISCLOSURE TEMENT BY APPLICANT (Use as many sheets as necessary) Filing Date First Named Inventor David S. F. Young Art Unit Examiner Name			
\subset	Sheet	1	of	-6	Attorney Docket Number	2056.025

			U. S. PATENT	T DOCUMENTS	
Examiner Initials*	Cite No.1	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant
	 	Number-Kind Code ^{2 (# known)}		 	Figures Appear
		^{US-} 5,869,045	02/09/1999	I. Hellstrom	
		^{US-} 5,869,268	02/09/1999	T. Kudo	
		^{US-} 5,849,876	12/15/1998	P. Linsley	
		^{US-} 5,783,186	07/21/1998	T. Arakawa	
		^{US-} 5,780,033	07/14/1998	V. Torchilin	
		^{US-} 5,750,102	05/12/1998	L. Eisenbach	
		^{US-} 5,693,763	12/02/1997	J. Codington	
		^{US-} 5,484,596	01/16/1996	M. Hanna	
		^{US-} 5,171,665	12/15/1992	I. Hellstrom	
		^{US-} 4,861,581	08/29/1989	A. Epstein	
		^{US-} 5,916,561	06/29/1999	G. Adolf	
		^{US-} 5,616,468	04/01/1997	M. Salmi	
		^{US-} 5,879,898	03/09/1999	D. Tarin	
		^{US-} 5,942,417	08/24/1999	J. Ni	
		us- 5,885,575	03/23/1999	P. Herrlich	
		us- 2003/0103985	06/05/2003	G. Adolf	
		US-			
		US-			
		US-	<u> </u>	 	

			IGN PATENT DOCL	IMENTS		
Examiner Initials*	Cite No.1	Foreign Patent Document	Publication Date	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages	
		Country Code ³ "Number ⁴ "Kind Code ⁵ (if known)	MM-DD-YYYY		Or Relevant Figures Appear	Τ'
		WO02/094879	11/28/2002	G. Adolf		
	,					
						L
	ľ		1	1	1	

Examiner		Date	
Signature	l l	Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03)

Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

	e for form 1449/PTO				Compl t if Known
Jubanua	310110111111-1-1-1011110			Application Numb r	
INFO	PRMATION	DIS	CLOSURE	Filing Date	Herewith
STA	TEMENT E	BY A	PPLICANT	First Named Inventor	David S. F. Young
	(Ușe as many she	ote se ni	eressan/)	Art Unit	
	(Osc as many she	C13 E3 77		Examiner Name	
Sheet	2	of	6	Attorney Docket Number	2056.025

Examiner Initials*	No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		M. ALLOUCHE et al, "Ligation of the CD44 Adhesion Molecule Inhibits Drug-Induced Apoptosis in Human Myeloid Leukemia Cells", Blood, 96(3):1187-1190 (August, 2000)	1
		I. BARSHACK et al, "CD44 Expression in Normal Adrenal Tissue and Adrenal Tumors", J. Clin. Pathol., 51:52-54 (1998)	J
		R. BREYER et al, "Disruption of Intracerebral Progression of C6 Rat Glioblastoma by in vivo Treatment with Anti-CD44 Monoclonal Antibody", J. Neurosurg., 92:140-149 (January, 2000)	j
		D. COLNOT et al, "Reinfusion of Unprocessed, Granulocyte Colony-Stimulating Factor-Stimulated Whole Blood Allows Dose Escalation of 186Relabeled Chimeric Monoclonal Antibody U36 Radioimmunotherapy in a Phase I Dose Escalation Study",	J
		Clin. Cancer Res., 8:3401-3406 (November, 2002)	
		D. COLNOT et al, "Radioimmunotherapy in Patients with Head and Neck Squamous Cells Carcinoma:Initial Experience", Head & Neck, 23:559-565 (July, 2001)	1
		D. COLNOT et al, "Phase I Therapy Study of 186Re-Labeled Chimeric Monoclonal Antibody U36 in Patients with Squamous Cell Carcinoma of the Head and Neck", J. Nucl. Med., 41:1999-2010 (December, 2000)	1
		D. COLNOT et al, "Evaluation of Limited Blood Sampling in a Preceding 99mTC-Labeled Diagnostic Study to Predict the Pharmacokinetics and Myelotoxicity of 186Re-cMAb U36 Radioimmunotherapy", J. Nucl. Med., 42(9):1364-1367 (September, 2001)	٩
		A. DAAR et al, "The Membrane Antigens of Human Colorectal Cancer Cells:Demonstration with Monoclonal Antibodies of Heterogeneity within and between Tumours and of Anomalous Expression of HLA-DR", Eur. J. Cancer Clin. Oncol.,	1
		19(2):209-220 (1983)	

Examiner	Date	
Signature	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03)
Approved for use through 07/31/2006, OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Substitut	te for form 1449/PTO				Complete if Known
Cossino	10 10 10 11 1 1 1 1 1 1 1			Application Number	
INFO	DRMATION	DIS	CLOSURE	Filing Date	Herewith
STA	TEMENT B	BY A	PPLICANT	First Named Inventor	David S. F. Young
[(Use as many she	ote ae n	ecessary)	Art Unit	
	lose as many sne	ets as n		Examiner Name	
Sheet	3	of	6	Attorney Docket Number	2056.025

Examiner	Cite	NON PATENT LITERATURE DOCUMENTS Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of	
Initials*	No.1	the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		R. DE BREE et al, "Selection of Monoclonal Antibody E48 IgG or U36 IgG for Adjuvant Radioimmunotherapy in Head and Neck Cancer Patients", British J. Cancer, 75(7):1049-1060 (1997)	,
		R. DE BREE et al, "Radioimmunoscintigraphy and Biodistribution of Technetium-99m-labeled Monoclonal Antibody U36 in Patients with Head and Neck Cancer", Clin. Can. Res., 1:591-598 (June, 1995)	1
,		S. DENNING et al, "Antibodies Against the CD44 p80, Lymphocyte Homing Receptor Molecule Augment Human Peripheral Blood T Cell Activation", J. Immunol., 144:7-15 (January, 1990)	1
		B. FLANAGAN et al, "Chemical Composition adn Tissue Distribution of the Human CDw44 Glycoprotein", Immunol., 67:167-175 (1989)	1
		S. FOX et al, "Normal Human Tissues, in Addition to Some Tumors, Express Multple Different CD44 Isoforms", Cancer Res., 54:4539-4546 (August, 1994)	
		U. GUNTHERT et al, "A New Variant of Glycoprotein CD44 Confers Metastatic Potential to Rat Carcinoma Cells", Cell, 65:13-24 (April, 1991)	1
		Y. GUO et al, "Inhibition of Human Melanoma Growth and Metastasis in vivo by Anti-CD44 Monoclonal Antibody", Cancer Res., 54:1561-1565 (March, 1994)	١
		K. HEIDER et al, "Differential Expression of CD44 Splice Variants in Intestinal- and Diffuse-Type Human Gastric Carcinomas and Normal Gastric Mucosa", Cancer Res., 53:4197-4203 (September, 1993)	þ
		K. HEIDER et al, "A Human Homologue of the Rat Metastasis-associated Variant of CD44 is Expressed in Colorectal Carcinomas and Adenomatous Polyps", J. Cell Biol., 120:227-233 (January 1993)	١
		K. HEIDER et al, "Splice Variants of the Cell Surface Glycoprotein CD44 Associated with Metastatic Tumour Cells are Expressed in Normal Tissues of Humans and Cynomolgus Monkeys", Eur J. Cancer, 31A(13/14):2385-2391 (1995)	\

Examiner	Date
Signature	Considered

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03) Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

	e for form 1449/PTO	9000011710			Complete if Kn wn
Substituti	9 101 101111 1449/F 10			Applicati n Numb r	
INFO	RMATION	DIS	CLOSURE	Filing Dat	Herewith
STA	TEMENT E	BY A	PPLICANT	First Named Inventor	David S. F. Young
	//	-4		Art Unit	
	(Use as many she	ets as n	ecessary)	Examiner Name	
Sheet	4	of	6	Attorney Docket Number	2056.025

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		K. HEIDER et al, "Characterization of a High-Affinity Monoclonal Antibody Specific for CD44v6 as Candidate for Immunotherapy of Squamous Cell Carcinomas", Cancer Immunol. Immunother., 43:245-253 (1996)	~
		S. JALKANEN et al, "Biochemical Properties of Glycoproteins Involved in Lymphocyte Recognition of High Endothelial Venules in Man", J. Immunol., 141:1615-1623 (September, 1988)	<i>a</i>
		S. KAYASTHA et al, "Expression of the Hyaluronan Receptor, CD44S, in Epithelial Ovarian Cancer is an Independent Predictor of Survival", Clin. Cancer Res., 5:1073-1076 (May, 1999)	f
		S. KENNEL et al, "CD44 Expression on Murine Tissues", J. Cell Science, 104:373-382 (1993)	
		M. KHOURSHEED et al, "Expression of CD44s in Human Colorectal Cancer", Pathology Oncology Research, 8(3):170-174 (2002)	ę
		G. KOOPMAN et al, "Activated Human Lymphocytes and Aggressive Non-Hodgkin's Lymphomas Express a Homologue of the Rat Metastasis-associated Variant of CD44", J. Exp. Med., 177:897-904 (April, 1993)	\
		M. KUPPNER et al, "Differential Expression of the CD44 Molecule in Human Brain Tumours", Int. J. Cancer, 50:572-577 (1992)	\
		C. MACKAY et al, "Expression and Modulation of CD44 Variant Isoforms in Humans", J. Cell Biol., 124:71-82 (January 1994)	\
		D. NAOR et al, "CD44 in Cancer", Critical Reviews in Clinical Laboratory Science, 39(6):527-579 (2002)	\
		H. PONTA et al, "CD44: from Adhesion Molecules to Signalling Regulators", Nature Reviews, Molecular Cell Biology, 4:33-45 (January, 2003)	`

Examiner	Date	
Signature	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1,98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03)

Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
a a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO		Complete if Known			
Substitute	e for form 1449/P10			Application Number	
INFO	INFORMATION DISCLOSURE			Filing Dat	Herewith
STATEMENT BY APPLICANT			PPLICANT	First Named Inventor	David S. F. Young
				Art Unit	
(Use as many sheets as necessary)			ecessary)	Examiner Name	
Sheet	5	of	6	Attorney Docket Number	2056.025

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		J. ROSS et al, "Expression of the CD44 Cell Adhesion Molecule in Urinary Bladder Transitional Cell Carcinoma", Mod. Pathol., 9(8):854-860 (1996)	Į
		M. SAMI et al, "Regulated Expression of Exon v6 Containing Isoforms of CD44 in Man: Downregulation During Malignant Transformation of Tumors of Squamocellular Origin", J. Cell Biol., 122(2):431-442 (July, 1993)	1
		A. SCHRIJVERS et al, "MAb U36, a Novel Monoclonal Antibody Successful in Immunotargeting of Squamous Cell Carcinoma of the Head and Neck", Cancer Res., 53:4383-4390 (September, 1993)	}
		S. SEITER et al, "Prevention of Tumor Metastasis Formation by Anti-Variant CD44", J. Exp. Med., 177:443-455 (February, 1993)	1
		Y. SHIMIZU et al, "Dual Role of the CD44 Molecule in T Cell Adhesion and Activation", J. Immunol., 143:2457-2463 (October, 1989)	í
•		T. STROBEL et al, "In Vivo Inhibition of CD44 Limits Intra-Abdominal Spread of a Human Ovarian Cancer Xenograft in Nude Mice: A Novel Role for CD44 in the Process of Peritoneal Implantation", Cancer Res., 57:1228-1232 (April, 1997)	ŧ
		J. STROOMER et al, "Safety and Biodistribution of 99mTechnetium-labeled Anti-CD44v6 Monoclonal Antibody BIWA 1 in Head and Neck Cancer Patients", Clin. Can. Res., 6:3046-3055 (August, 2000)	\
		N. VAN HAL et al, "Monoclonal Antibody U36, a Suitable Candidate for Clinical Immunotherapy of Squamous-Cell Carcinoma, Recognizes a CD44 Isoform", Int. J. Cancer, 68:520-527 (1996)	ť
		S. WALLACH-DAYAN et al, "CD44-Dependent Lymphoma Cell Dissemination:a Cell Surface CD44 Variant, Rather than Standard CD44, Supports in vitro Lymphoma Cell Rolling on Hyaluronic Acid Substrate and its in vivo Accumulation in the Peripheral	\
		Lymph Nodes", J. Cell Science, 114:3463-3477 (2001)	

Examiner	Date	
Signature	Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
b a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO		Complete if Known			
Substitut	e for form 1449/P10			Applicati n Numb r	
INFO	DRMATION	N DIS	CLOSURE	Filing Dat	Herewith
STATEMENT BY APPLICANT			PPLICANT	First Named Inventor	David S. F. Young
				Art Unit	
	(Use as many sh	eets as ne	cessary)	Examiner Name	
Sheet	6	of	6	Attorney Docket Number	2056.025

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		M. ZAHALKA et al, "Lymph Node (but not spleen) Invasion by Murine Lymphoma is both CD44- and Hyaluronate-Dependent", J. Immunol., 154:5345-5355 (1995)	
		V. ZAWADZKI et al, "Blockade of Metastasis Formation by CD44-Receptor Globulin", Int. J. Cancer, 75:919-924 (1998)	

Examiner	Date
Signature	Considered

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation in the information and the considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.